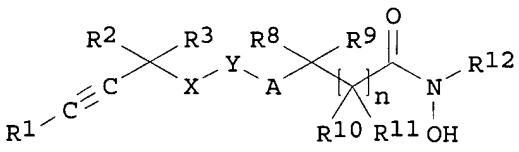
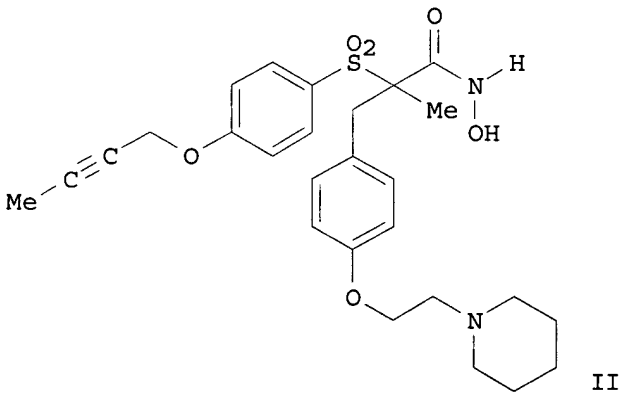
AN 2000:535106 CAPLUS
DN 133:150348
TI Preparation of alkynyl containing hydroxamic acid compounds as TACE inhibitors
IN Levin, Jeremy Ian; Venkatesan, Aranapakam Mudumbai; Cole, Derek Cecil; Chen, James Ming; Davis, Jamie Marie; Grosu, George Theodore
PA American Cyanamid Company, USA
SO PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000044713	A1	20000803	WO 2000-US2078	20000127
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1147080	A1	20011024	EP 2000-911652	20000127
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	BR 2000007783	A	20020205	BR 2000-7783	20000127
	NO 2001003677	A	20010920	NO 2001-3677	20010726
PRAI	US 1999-239088	A	19990127		
	WO 2000-US2078	W	20000127		

OS MARPAT 133:150348
GI



I



II

AB The title compds. [I; R1 = H, aryl, heteroaryl, etc.; R2, R3 = H, alkyl, CN, CCH; R8-R11 = H, aryl, aralkyl, etc.; R12 = H, aryl, 5-10 membered heteroaryl having 1-3 heteroatoms selected from N, S, O, etc.; A = O, S, SO, etc.; X = O, S, SO, etc.; Y = aryl, heteroaryl, with the proviso that A and X are not bonded to adjacent atoms of Y; n = 0-2] and their pharmaceutically acceptable salts, useful in treating disease conditions mediated by TNF-.alpha., such as rheumatoid arthritis, osteoarthritis, sepsis, AIDS, ulcerative colitis, multiple sclerosis, Crohn's disease and degenerative cartilage loss, were prepd. E.g., a multi-step synthesis of II.HCl which showed IC50 of 191 nM against TACE, and IC50 of 2 nM, 180 nM, and 200 nM against MMP-1, MMP-9, and MMP-13, resp., was given.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

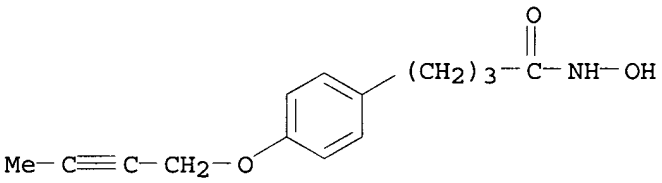
=> d hitstr 2

L17 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS

IT **287391-54-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of alkynyl contg. hydroxamic acid compds. as TACE inhibitors)

RN 287391-54-2 CAPLUS

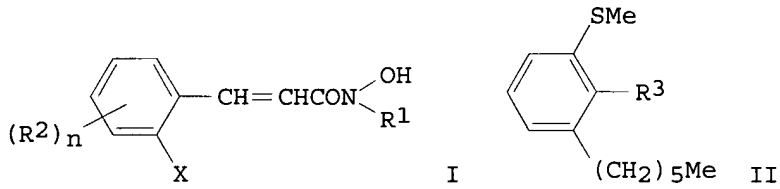
CN Benzenebutanamide, 4-(2-butynyloxy)-N-hydroxy- (9CI) (CA INDEX NAME)



AN 1991:582857 CAPLUS
DN 115:182857
TI Preparation of N-hydroxy-N-alkylcinnamides as 5-lipoxygenase inhibitors
IN Hite, Gary A.; Mihelich, Edward D.; Suarez, Tulio
PA Lilly, Eli, and Co., USA
SO U.S., 18 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5028629	A	19910702	US 1990-500820	19900328
PRAI US 1990-500820		19900328		

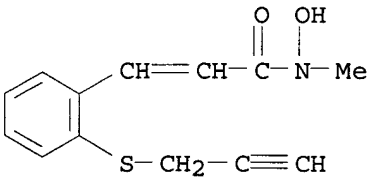
OS MARPAT 115:182857
GI



AB The title amides [I; R1 = C1-4 alkyl; R2 = CF3, C1-10 alkyl, RS(O)m (wherein R = C1-4 alkyl; m = 0-2); X = C1-6 alkyl, (substituted) Ph, etc.; n = 0, 1] are prepd. Oxidn. of aldehyde II (R2 = CHO) with Me3SiCH2CO2CMe3 and LiN(CHMe2)2 in THF gave the acid II (R3 = CO2H), which was treated with oxalyl chloride in DMF under cooling and the resultant acid chloride was treated with MeNHOH.HCl and Et3N in THF-H2O under cooling and at room temp. to give I (R1 = Me, R2 = 6-MeS, X = hexyl, n = 1). Also prepd. were 45 addnl. I which showed 5-lipoxygenase and polymorphonuclear leukocyte inhibition of a concn. as low as 0.07 .mu.M. Tablet, capsule, aerosol suspension, etc. formulations were given.

IT **136516-15-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as lipoxygenase inhibitor)

RN 136516-15-9 CAPLUS
CN 2-Propenamide, N-hydroxy-N-methyl-3-[2-(2-propynylthio)phenyl]- (9CI) (CA INDEX NAME)



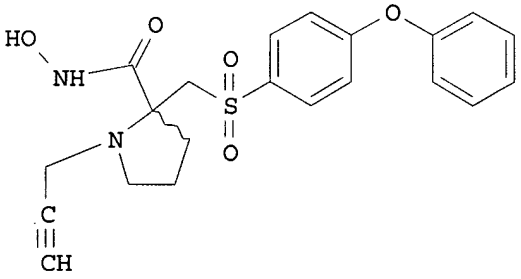
AN 2001:886852 CAPLUS
DN 136:20008
TI Preparation of aromatic sulfonyl alpha-cycloamino hydroxamates as MMP inhibitors
IN Becker, Daniel P.; Li, Madeleine H.; DeCrescenzo, Gary A.
PA USA
SO U.S. Pat. Appl. Publ., 13 pp., Cont.-in-part of U.S. Ser. No. 254,530, abandoned.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2001049449	A1	20011206	US 2001-778411	20010207 <--
WO 2002062756	A1	20020815	WO 2002-US3448	20020207

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-254530 B2 19991223
US 2001-778411 A 20010207
OS MARPAT 136:20008
GI



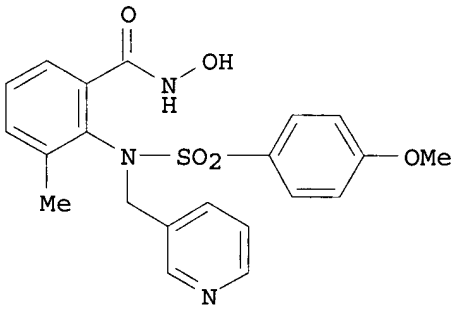
I

AB Arom. sulfonyl alpha-cycloamino hydroxamic acid compds. (I), and pharmaceutically acceptable salts thereof, that inhibit matrix metalloprotease activity, are disclosed. Thus, N-hydroxy-2-[[(4-phenoxyphenyl)sulfonyl]methyl]-1-(2-propynyl)-2-**pyrrolidine** carboxamide monohydrochloride was prepd. in several steps. Inhibition of **MMP**-1, **MMP**-2, and **MMP**-13 by I was detd.

AN 1998:251153 CAPLUS
DN 128:308308
TI The preparation and use of ortho-sulfonamido aryl hydroxamic acids as matrix metalloproteinase and TACE inhibitors
IN Levin, Jeremy Ian; Du Mila, T.; Venkatesan, Aranapakam Mudumbai; Nelson, Frances Christy; Zask, Arie; Gu, Yansong
PA American Cyanamid Company, USA
SO PCT Int. Appl., 164 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9816503	A2	19980423	WO 1997-US18280	19971008	<--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW					
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	AU 9851458	A1	19980511	AU 1998-51458	19971008	<--
	AU 731737	B2	20010405			
	EP 938471	A1	19990901	EP 1997-946246	19971008	
	EP 938471	B1	20011212			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO					
	BR 9712525	A	19991019	BR 1997-12525	19971008	
	CN 1240429	A	20000105	CN 1997-180613	19971008	
	JP 2001504809	T2	20010410	JP 1998-518448	19971008	
	AT 210637	E	20011215	AT 1997-946246	19971008	
	ES 2166102	T3	20020401	ES 1997-946246	19971008	
	ZA 9709233	A	19990415	ZA 1997-9233	19971015	
	TW 410220	B	20001101	TW 1997-86114187	19971015	
	KR 2000049196	A	20000725	KR 1999-703294	19990415	
PRAI	US 1996-732631	A	19961016			
	WO 1997-US18280	W	19971008			

OS MARPAT 128:308308
GI



II

AB The invention relates to novel, low mol. wt., non-peptide inhibitors of matrix metalloproteinases (e.g. gelatinases, stromelysins and collagenases) and TNF-.alpha. converting enzyme (TACE, tumor necrosis factor-.alpha. converting enzyme). The compds. are useful for the treatment of diseases in which these enzymes are implicated such as

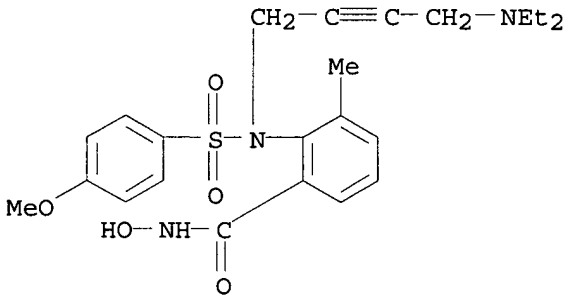
arthritis, tumor growth and metastasis, angiogenesis, tissue ulceration, abnormal wound healing, periodontal disease, bone disease, proteinuria, aneurysmal aortic disease, degenerative cartilage loss following traumatic joint injury, demyelinating diseases of the nervous system, graft rejection, cachexia, anorexia, inflammation, fever, insulin resistance, septic shock, congestive heart failure, inflammatory disease of the central nervous system, inflammatory bowel disease, HIV infection, age related macular degeneration, diabetic retinopathy, proliferative vitreoretinopathy, retinopathy of prematurity, ocular inflammation, keratoconus, Sjogren's syndrome, myopia, ocular tumors, and ocular angiogenesis/neovascularization. The invention compds. are represented by the formula ZSO2N(CH2R7)ACONHOH [I; A = (un)substituted Ph or naphthyl; Z = (un)substituted aryl, heteroaryl, or benzo-fused heteroaryl; R7 = H, (un)substituted alk(en/yn)yl, Ph, naphthyl, 5- or 6-membered heteroaryl, cycloalkyl, or cycloheteroalkyl; or R7CH2NA forms a non-arom. 1,2-benzo-fused 7- to 10-membered heterocyclic ring with an optional addn. benzo fusion; where the hydroxamic acid moiety and the sulfonamido moiety are bonded to adjacent carbons on group A], and include pharmaceutically acceptable salts, optical isomers, and diastereomers. Prepns. of over 400 compds., including I and their intermediates, are given. For instance, 2-[(4-methoxybenzenesulfonyl)amino]-3-methylbenzoic acid Me ester (prepn. given) was N-alkylated by 3-picolyl chloride-HCl (83%), followed by hydrolysis of the ester with LiOH in aq. THF (100%), activation with oxalyl chloride, and hydroxamidation with NH2OH.HCl (51%), to give title compd. II. At 50 mg/kg/day in rats with cartilage implants, II gave 44.6% inhibition of cartilage wt. loss, and 51.2% inhibition of cartilage collagen loss.

IT **206550-54-1P 206551-87-3P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of ortho-sulfonamido aryl hydroxamic acids as matrix metalloproteinase and TACE inhibitors)

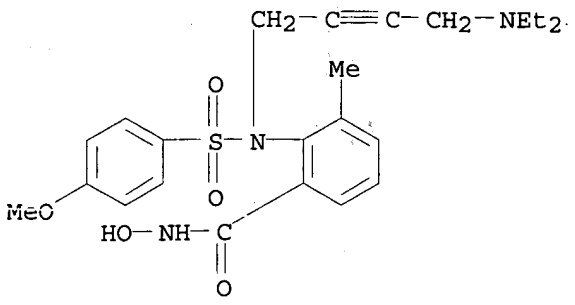
RN 206550-54-1 CAPLUS

CN Benzamide, 2-[[4-(diethylamino)-2-butynyl][(4-methoxyphenyl)sulfonyl]amino]-N-hydroxy-3-methyl- (9CI) (CA INDEX NAME)



RN 206551-87-3 CAPLUS

CN Benzamide, 2-[[4-(diethylamino)-2-butynyl][(4-methoxyphenyl)sulfonyl]amino]-N-hydroxy-3-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl